Functional and connectivity asymmetry observed in the visual system of an infant with white matter lesions on MRI

M. A. Dresner[1], S. J. Counsell[1], L. Srinivasan[1,2], R. M. Raafat[1], F. M. Cowan[2], J. M. Allsop[1], M. A. Rutherford[1,2], J. V. Hajnal[1], A. D. Edwards[1,2]

[1]Robert Steiner MRI Unit, Imaging Sciences Department, MRC Clinical Sciences Centre, Imperial College London, London, United Kingdom, [2]Department of Paediatrics, Imaging Sciences Department, MRC Clinical Sciences Centre, Hammersmith Hospital, London, United Kingdom

Introduction

The incidence of periventricular leukomalacia (PVL) and periventricular haemorrhagic infarction (PHI) has declined in recent years. However, they remain the major destructive focal lesions affecting the preterm brain and are associated with significant motor and, in infants with PVL, visual impairment.[1-4] Recently, functional MRI (fMRI) and diffusion tractography have been combined to assess the structure-functional relationship following perinatal stroke.[5] Here we present the case of an infant who was born preterm with evidence of PVL and PHI who was serially assessed using conventional MRI, and who underwent fMRI and DTI at 25 months corrected age.

Methods

Ethical approval for this study was granted by the local Research Ethics Committee and written parental consent was obtained prior to scanning. This male infant was born at 27^{+2} weeks gestational age with a birthweight of 836 grams. MRI was obtained at term corrected age (41 weeks post-menstrual age (pma)), 13 months corrected age and again at 25 months corrected age. In addition to conventional imaging, fMRI and DTI were obtained at 25 months corrected age, using a Philips 3T system and standard 6 channel head coil. The infant was imaged after sedation with oral chloral hydrate to prevent image degradation from motion artefacts. Ear protection was implemented with silicon-based dental putty and mini-muffs, and the subject's head was immobilised using a vacuum pillow.

fMRI: The fMRI data were acquired using 2-D multi-slice EPI scans (TE/TR/θ 30/3000/90, 34 slices, 128 matrix and 260 mm FOV). The fMRI lights paradigm consisted of 5 blocks of 8 scans (24 seconds) with scanner gantry lights manually cycled at 1 Hz alternating with 5 blocks of 8 scans of darkness, with 5 scans before and after the paradigm to reach steady-state magnetization and capture the last haemodynamic response, respectively. Second-order shim gradients and SENSE factor 2 were applied to reduce the susceptibility-based losses that occur with echo-planar imaging at 3 Tesla. EPI scans were performed in a reduced acoustic noise mode with gradient slew rates and amplitudes reduced, at the expense of echo spacing. Functional data were analysed with SPM2 (Wellcome Institute, London); pre-processing of EPI data included spatial realignment and smoothing with an isotropic Gaussian kernel of 6 mm FWHM. Subject motions estimated in the realignment stage were used as additional regressors to capture movement-related variance.

DTI: Single shot EPI DTI was acquired in 15 non-colinear directions using the following parameters; TR 9000ms, TE 49ms, slice thickness 2mm, field of view 224mm, matrix 128 x 128 (voxel size = 1.75 x 1.75 x 2 mm^3), 2 NSA, *b* value = 1000 s/mm^2. The data were acquired with a SENSE factor of 2 and the DTI scan time was ~7 minutes. Connectivity distributions in the optic radiations were assessed using the FMRIB diffusion toolkit (FDT).[6] DTI and fMRI results were coregistered to the T2-weighted structural scans.

Results

Neonatal imaging demonstrated a large porencephalic cyst on the right with bilateral ventricular dilatation, right > left (figure 1). At 13 months corrected age, the posterior horns of the lateral ventricles appeared "squared", and there was increased T2 in the occipital white matter. The thalamus appeared atrophied on the right side. These findings persisted at 25 months corrected age (figure 2). fMRI scan analysis showed activation on both left and right, with larger activation on the left. The activations are shown in blue (figure 3, overlaid on co-registered T2-weighted image FWE corrected at $p<0.05$) reflecting the characteristic 'negative signal' of sedated infant fMRI[5,7]. Probabilistic tractography demonstrated asymmetrical connectivity distributions in the optic radiation (figure 3). The child has a left sided hemiplegia consistent with the right sided lesion and has global developmental delays, with no major visual impairment.

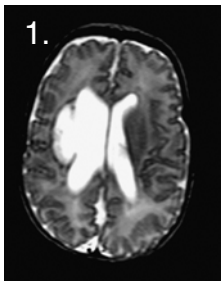

Figure 1. T2 weighted imaging obtained at 41 weeks pma demonstrating right porencephalic cyst and bilateral ventricular dilatation.

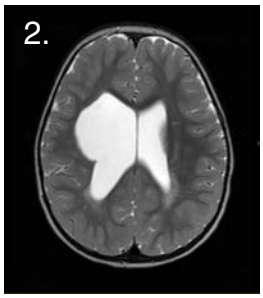

Figure 2. T2 weighted imaging obtained at 25 months corrected age.

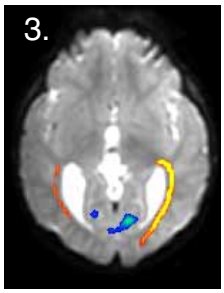

Figure 3. MIP of connectivity distributions in the optic radiations and functional activation ($p< 0.05$) overlaid on anatomical section.

Discussion

Combining fMRI and diffusion tractography enables structure and activation in human brain to be assessed non-invasively. Furthermore, the increased signal to noise ratio offered by imaging at 3 Tesla provides robust functional activation, which is beneficial when imaging infants. Here we were able to demonstrate asymmetrical fMRI activation in the visual cortex in correlation with asymmetrical connectivity in the optic radiations, as assessed by probabilistic tractography, in an infant who was born preterm and developed white matter lesions. Of interest, no visual impairment was apparent in the paediatric clinic setting, despite imaging evidence of diminished connectivity on the right. More detailed visual testing will be performed as this child gets older.

References

1. De Vries et al. *Neuropediatrics*, 1987; 18: 61-6. 2. Scher et al. *Dev Med Child Neurol*, 1989; 31: 353-65. 3. Cioni et al. *Pediatr Neurol*, 1997; 17: 331-8. 4. van der Hout et al. *Dev Med Child Neurol*, 2000; 42: 376-86. 5. Seghier et al. *BMC Neurology*, 2005; 7:17 6. Behrens et al. *Nature Neuroscience* 2003; 6: 750-7. 7. Born et al. *Pediatric Research*, 1998, 44: 578-83.

Acknowledgements

We are grateful to Philips Medical Systems, Medical Research Council (UK) and The Health Foundation for research grant support.